

What is claimed is:

- 5 1. An isolated nucleic acid encoding a human MCH1 receptor or a mutant of such human MCH1 receptor which is activated by MCH or an analog or homolog thereof.
- 10 2. The nucleic acid of claim 1, wherein the nucleic acid is DNA.
3. The DNA of claim 2, wherein the DNA is cDNA.
4. The DNA of claim 2, wherein the DNA is genomic DNA.
- 15 5. The nucleic acid of claim 1, wherein the nucleic acid is RNA.
- 20 6. The nucleic acid of claim 1, wherein the human MCH1 receptor has an amino acid sequence identical to that encoded by the plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197).
- 25 7. The nucleic acid of claim 1, wherein the human MCH1 receptor comprises an amino acid sequence as shown in Figure 2 (SEQ ID NO: 2).
- 30 8. The nucleic acid of claim 1, wherein the mutant human MCH1 receptor comprises an amino acid sequence as shown in Figure 13 (SEQ ID NO: 26).
9. The nucleic acid of claim 1, wherein the mutant human MCH1 receptor comprises an amino acid sequence as shown in Figure 14 (SEQ ID NO: 27).
- 35 10. The nucleic acid of claim 1, wherein the mutant human

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Figure 15 (SEQ ID NO  
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so as to permit expr  
is a bacterial, amph  
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r of claim 13, wh  
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r of claim 12, wh

d of claim 15 design  
No. 203197).

nprising the vector

f claim 17, wherei  
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claim 18, wherein th  
oocyte cell or a Xe

claim 17, wherein

11. A purified human MCH1 receptor protein.
12. A vector comprising the nucleic acid of claim 1.
13. The vector of claim 12 adapted for expression in a cell which comprises the regulatory elements necessary for expression of the nucleic acid in the cell operatively linked to the nucleic acid encoding the receptor so as to permit expression thereof, wherein the cell is a bacterial, amphibian, yeast, insect or mammalian cell.
14. The vector of claim 13, wherein the vector is a baculovirus.
15. The vector of claim 12, wherein the vector is a plasmid.
16. The plasmid of claim 15 designated pEXJ.HR-TL231 (ATCC Accession No. 203197).
17. A cell comprising the vector of claim 13.
18. A cell of claim 17, wherein the cell is a non-mammalian cell.
19. A cell of claim 18, wherein the non-mammalian cell is a *Xenopus* oocyte cell or a *Xenopus* melanophore cell.
20. A cell of claim 17, wherein the cell is a mammalian cell.

21. A mammalian cell of claim 20, wherein the cell is a COS-7 cell, a 293 human embryonic kidney cell, a NIH-3T3 cell, a LM(tk-) cell, a mouse Y1 cell, or a CHO cell.
22. An insect cell comprising the vector of claim 13.
23. An insect cell of claim 22, wherein the insect cell is an Sf9 cell, an Sf21 cell or a Trichoplusia ni 5B-4 cell.
24. A membrane preparation isolated from the cell of claim 17.
25. A nucleic acid probe comprising at least 15 nucleotides which specifically hybridizes with a nucleic acid encoding a human MCH1 receptor, wherein the probe has a unique sequence corresponding to a sequence present within one of the two strands of the nucleic acid encoding a human MCH1 receptor present in plasmid pEXJ.HR-T231 (ATCC Accession No. 203197).
26. A nucleic acid probe comprising at least 15 nucleotides which specifically hybridizes with a nucleic acid encoding a human MCH1 receptor, wherein the probe has a unique sequence corresponding to a sequence present within (a) the nucleic acid sequence shown in Figure 1 (SEQ ID NO: 1) or (b) the reverse complement thereof.
27. The nucleic acid probe of claim 25 or 26, wherein the nucleic acid is DNA.
28. The nucleic acid probe of claim 25 or 26, wherein the nucleic acid is RNA.

29. An antisense oligonucleotide having a sequence capable of specifically hybridizing to the RNA of claim 5, so as to prevent translation of the RNA.
- 5 30. An antisense oligonucleotide having a sequence capable of specifically hybridizing to the genomic DNA of claim 4.
- 10 31. An antisense oligonucleotide of claim 29 or 30, wherein the oligonucleotide comprises chemically modified nucleotides or nucleotide analogues.
- 15 32. An antibody capable of binding to a human MCH1 receptor encoded by the nucleic acid of claim 1.
- 20 33. An agent capable of competitively inhibiting the binding of the antibody of claim 32 to a human MCH1 receptor.
- 25 34. An antibody of claim 32, wherein the antibody is a monoclonal antibody or antisera.
- 30 35. A pharmaceutical composition comprising (a) an amount of the oligonucleotide of claim 29 capable of passing through a cell membrane and effective to reduce expression of a human MCH1 receptor and (b) a pharmaceutically acceptable carrier capable of passing through the cell membrane.
- 35 36. A pharmaceutical composition of claim 35, wherein the oligonucleotide is coupled to a substance which inactivates mRNA.
37. A pharmaceutical composition of claim 36, wherein the substance which inactivates mRNA is a ribozyme.

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38. A pharmaceutical composition of claim 35, wherein the pharmaceutically acceptable carrier comprises a structure which binds to a human MCH1 receptor on a cell capable of being taken up by the cells after binding to the structure.
39. A pharmaceutical composition of claim 35, wherein the pharmaceutically acceptable carrier is capable of binding to a human MCH1 receptor which is specific for a selected cell type.
40. A pharmaceutical composition which comprises an amount of the antibody of claim 32 effective to block binding of a ligand to a human MCH1 receptor and a pharmaceutically acceptable carrier.
41. A transgenic, nonhuman mammal expressing DNA encoding a human MCH1 receptor of claim 1.
42. A transgenic, nonhuman mammal comprising a homologous recombination knockout of the native human MCH1 receptor.
43. A transgenic, nonhuman mammal whose genome comprises antisense DNA complementary to the DNA encoding a human MCH1 receptor of claim 1 so placed within the genome as to be transcribed into antisense mRNA which is complementary to mRNA encoding the human MCH1 receptor and which hybridizes to mRNA encoding the human MCH1 receptor, thereby reducing its translation.
44. The transgenic, nonhuman mammal of claim 41 or 42, wherein the DNA encoding the human MCH1 receptor additionally comprises an inducible promoter.

45. The transgenic, nonhuman mammal of claim 41 or 42, wherein the DNA encoding the human MCH1 receptor additionally comprises tissue specific regulatory elements.
46. A transgenic, nonhuman mammal of claim 41, 42, or 43, wherein the transgenic, nonhuman mammal is a mouse.
47. A process for identifying a chemical compound which specifically binds to a mammalian MCH1 receptor which comprises contacting cells comprising DNA encoding, and expressing on their cell surface, the mammalian MCH1 receptor, with the compound under conditions suitable for binding, and detecting specific binding of the chemical compound to the mammalian MCH1 receptor, wherein the cells do not normally express the mammalian MCH1 receptor and the DNA encoding the mammalian MCH1 receptor (a) hybridizes to a nucleic acid having the defined sequence shown in Figure 1 (SEQ ID NO: 1) under low stringency conditions or a sequence complementary thereto and (b) is further characterized by its ability to cause a change in the pH of a culture of CHO cells when a MCH1 ligand is added to the culture and the CHO cells contain the nucleic acid which hybridized to the nucleic acid having the defined sequence or its complement.
48. A process for identifying a chemical compound which specifically binds to a mammalian MCH1 receptor which comprises contacting a membrane preparation from cells comprising DNA encoding, and expressing on their cell surface, the mammalian MCH1 receptor, with the compound under conditions suitable for binding, and detecting specific binding of the chemical compound to the mammalian MCH1 receptor, wherein the cells do not

normally express the mammalian MCH1 receptor and the DNA encoding the mammalian MCH1 receptor (a) hybridizes to a nucleic acid having the defined sequence shown in Figure 1 (SEQ ID NO: 1) under low stringency conditions or a sequence complementary thereto and (b) is further characterized by its ability to cause a change in the pH of a culture of CHO cells when a MCH1 ligand is added to the culture and the CHO cells contain the nucleic acid which hybridized to the nucleic acid having the defined sequence or its complement.

49. The process of claim 47 or 48, wherein the mammalian MCH1 receptor is a human MCH1 receptor.

50. The process of claim 47 or 48, wherein the mammalian MCH1 receptor is a rat MCH1 receptor.

51. The process of claim 47 or 48, wherein the mammalian MCH1 receptor has substantially the same amino acid sequence as the sequence of the human MCH1 receptor encoded by plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197).

52. The process of claim 47 or 48, wherein the mammalian MCH1 receptor comprises substantially the same amino acid sequence as that shown in Figure 2 (SEQ ID NO: 2).

53. The process of claim 47 or 48, wherein the mammalian MCH1 receptor comprises the amino acid sequence shown in Figure 2 (SEQ ID NO: 2).

54. The process of claim 47 or 48, wherein the mammalian MCH1 receptor comprises the amino acid sequence shown

in Figure 13 (SEQ ID NO: 26).

55. The process of claim 47 or 48, wherein the mammalian MCH1 receptor comprises the amino acid sequence shown in Figure 14 (SEQ ID NO: 27).

56. The process of claim 47 or 48, wherein the mammalian MCH1 receptor comprises the amino acid sequence shown in Figure 15 (SEQ ID NO: 28).

57. The process of claim 47 or 48, wherein the compound is not previously known to bind to a mammalian MCH1 receptor.

58. A compound identified by the process of claim 57.

59. A process of claim 47 or 48, wherein the cell is an insect cell.

60. The process of claim 47 or 48, wherein the cell is a mammalian cell.

61. The process of claim 60, wherein the cell is nonneuronal in origin.

62. The process of claim 61, wherein the nonneuronal cell is a COS-7 cell, 293 human embryonic kidney cell, a CHO cell, a NIH-3T3 cell, a mouse Y1 cell, or a LM(tk-) cell.

63. A process of claim 60, wherein the compound is a compound not previously known to bind to a mammalian MCH1 receptor.

64. A compound identified by the process of claim 63.

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66. A process involving competitive binding for identifying a chemical compound which specifically binds to a mammalian MCH1 receptor which comprises contacting a membrane preparation from cells expressing on their cell surface the mammalian MCH1 receptor, with both the chemical compound and a second chemical compound known to bind to the receptor, and separately with only the second chemical compound, under conditions suitable for binding of both

compounds, and detecting specific binding of the chemical compound to the mammalian MCH1 receptor, a decrease in the binding of the second chemical compound to the mammalian MCH1 receptor in the presence of the chemical compound indicating that the chemical compound binds to the mammalian MCH1 receptor, wherein the cells do not normally express the mammalian MCH1 receptor and the DNA encoding the mammalian MCH1 receptor (a) hybridizes to a nucleic acid having the defined sequence shown in Figure 1 (SEQ ID NO: 1) under low stringency conditions or a sequence complementary thereto and (b) is further characterized by its ability to cause a change in the pH of a culture of CHO cells when a MCH1 ligand is added to the culture and the CHO cells contain the nucleic acid which hybridized to the nucleic acid having the defined sequence or its complement.

67. A process of claim 65 or 66, wherein the mammalian MCH1 receptor is a human MCH1 receptor or a mutant of such human MCH1 receptor which is activated by MCH or an analog or homolog thereof.

68. A process of claim 65 or 66, wherein the mammalian MCH1 receptor is a rat MCH1 receptor.

69. The process of claim 65 or 66, wherein the cell is an insect cell.

70. The process of claim 65 or 66, wherein the cell is a mammalian cell.

71. The process of claim 70, wherein the cell is nonneuronal in origin.

72. The process of claim 71, wherein the nonneuronal cell is a COS-7 cell, 293 human embryonic kidney cell, a CHO cell, a NIH-3T3 cell, a mouse Y1 cell, or a LM(tk-) cell.

73. The process of claim 70, wherein the compound is not previously known to bind to a mammalian MCH1 receptor.

74. A compound identified by the process of claim 73.

75. A method of screening a plurality of chemical compounds not known to bind to a mammalian MCH1 receptor to identify a compound which specifically binds to the mammalian MCH1 receptor, which comprises

(a) contacting cells transfected with and expressing DNA encoding the mammalian MCH1 receptor with the plurality of compounds not known to bind specifically to the mammalian MCH1 receptor, under conditions permitting binding of compounds known to bind the mammalian MCH1 receptor;

(b) determining whether the binding of a compound known to bind to the mammalian MCH1 receptor is reduced in the presence of the compounds within the plurality of compounds, relative to the binding of the compound in the absence of the plurality of compounds; and if so

(c) separately determining the binding to the mammalian MCH1 receptor of compounds included in the plurality of compounds, so as to thereby identify the compound which specifically binds to the mammalian MCH1

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receptor.

76. A method of screening a plurality of chemical compounds not known to bind to a mammalian MCH1 receptor to identify a compound which specifically binds to the mammalian MCH1 receptor, which comprises

(a) contacting a membrane preparation from cells transfected with and expressing DNA encoding the mammalian MCH1 receptor with the plurality of compounds not known to bind specifically to the mammalian MCH1 receptor under conditions permitting binding of compounds known to bind the mammalian MCH1 receptor;

(b) determining whether the binding of a compound known to bind to the mammalian MCH1 receptor is reduced in the presence of the compounds within the plurality of compounds, relative to the binding of the compound in the absence of the plurality of compounds; and if so

(c) separately determining the binding to the mammalian MCH1 receptor of compounds included in the plurality of compounds, so as to thereby identify the compound which specifically binds to the mammalian MCH1 receptor.

77. A method of claim 75 or 76, wherein the mammalian MCH1 receptor is a human MCH1 receptor or a mutant of such human MCH1 receptor which is activated by MCH or an analog or homolog thereof.

78. A method of claim 75 or 76, wherein the mammalian MCH1 receptor is a rat MCH1 receptor.
79. A method of claim 75 or 76, wherein the cell is a mammalian cell.
80. A method of claim 79, wherein the mammalian cell is non-neuronal in origin.
81. The method of claim 80, wherein the non-neuronal cell is a COS-7 cell, a 293 human embryonic kidney cell, a LM(tk-) cell, a CHO cell, a mouse Y1 cell, or an NIH-3T3 cell.
82. A method of detecting expression of a mammalian MCH1 receptor by detecting the presence of mRNA coding for the mammalian MCH1 receptor which comprises obtaining total mRNA from the cell and contacting the mRNA so obtained with the nucleic acid probe of any of claims 25, 26, 27, or 28 under hybridizing conditions, detecting the presence of mRNA hybridizing to the probe, and thereby detecting the expression of the mammalian MCH1 receptor by the cell.
83. A method of detecting the presence of a mammalian MCH1 receptor on the surface of a cell which comprises contacting the cell with the antibody of claim 32 under conditions permitting binding of the antibody to the receptor, detecting the presence of the antibody bound to the cell, and thereby detecting the presence of the mammalian MCH1 receptor on the surface of the cell.
84. A method of determining the physiological effects of varying levels of activity of human MCH1 receptors

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which comprises producing a transgenic, nonhuman mammal of claim 44 whose levels of human MCH1 receptor activity are varied by use of an inducible promoter which regulates human MCH1 receptor expression.

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85. A method of determining the physiological effects of varying levels of activity of human MCH1 receptors which comprises producing a panel of transgenic, nonhuman mammals of claim 44, each expressing a different amount of human MCH1 receptor.

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86. A method for identifying an antagonist capable of alleviating an abnormality, wherein the abnormality is alleviated by decreasing the activity of a human MCH1 receptor comprising administering a compound to the transgenic, nonhuman mammal of claim 41, 44, 45, or 46, and determining whether the compound alleviates the physical and behavioral abnormalities displayed by the transgenic, nonhuman mammal as a result of overactivity of a human MCH1 receptor, the alleviation of the abnormality identifying the compound as an antagonist.

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87. An antagonist identified by the method of claim 86.

88. A pharmaceutical composition comprising an antagonist of claim 87 and a pharmaceutically acceptable carrier.

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89. A method of treating an abnormality in a subject wherein the abnormality is alleviated by decreasing the activity of a human MCH1 receptor which comprises administering to the subject an effective amount of the pharmaceutical composition of claim 88, thereby treating the abnormality.

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(c) electrophoretically separating the resulting DNA fragments on a sizing gel;

(d) contacting the resulting gel with a nucleic acid probe capable of specifically hybridizing with a unique sequence included within the sequence of a nucleic acid molecule encoding a human MCH1 receptor and labeled with a detectable marker;

(e) detecting labeled bands which have hybridized to the DNA encoding a human MCH1 receptor of claim 1 labeled with a detectable marker to create a unique band pattern specific to the DNA of subjects suffering from the disorder;

(f) preparing DNA obtained for diagnosis by steps (a)-(e); and

(g) comparing the unique band pattern specific to the DNA of subjects suffering from the disorder from step (e) and the DNA obtained for diagnosis from step (f) to determine whether the patterns are the same or different and to diagnose thereby predisposition to the disorder if the patterns are the same.

95. The method of claim 94, wherein a disorder associated with the activity of a specific mammalian allele is diagnosed.

96. A method of preparing the purified human MCH1 receptor of claim 11 which comprises:

(a) inducing cells to express the human MCH1 receptor;

(b) recovering the human MCH1 receptor from the induced cells; and

(c) purifying the human MCH1 receptor so recovered.

97. A method of preparing the purified human MCH1 receptor of claim 11 which comprises:

(a) inserting nucleic acid encoding the human MCH1 receptor in a suitable vector;

(b) introducing the resulting vector in a suitable host cell;

(c) placing the resulting cell in suitable condition permitting the production of the isolated human MCH1 receptor;

(d) recovering the human MCH1 receptor produced by the resulting cell; and

(e) purifying the human MCH1 receptor so recovered.

98. A process for determining whether a chemical compound is a mammalian MCH1 receptor agonist which comprises contacting cells transfected with and expressing DNA encoding the mammalian MCH1 receptor with the compound under conditions permitting the activation of the mammalian MCH1 receptor, and detecting an increase in mammalian MCH1 receptor activity, so as to thereby determine whether the compound is a mammalian MCH1 receptor agonist.

5 99. A process for determining whether a chemical compound  
is a mammalian MCH1 receptor antagonist which  
comprises contacting cells transfected with and  
expressing DNA encoding the mammalian MCH1 receptor  
with the compound in the presence of a known mammalian  
MCH1 receptor agonist, under conditions permitting the  
activation of the mammalian MCH1 receptor, and  
detecting a decrease in mammalian MCH1 receptor  
activity, so as to thereby determine whether the  
10 compound is a mammalian MCH1 receptor antagonist.

15 100. A process of claim 98 or 99, wherein the mammalian  
MCH1 receptor is a human MCH1 receptor or a mutant  
of such human MCH1 receptor which is activated by  
MCH or an analog or homolog thereof.

20 101. A process of claim 98 or 99, wherein the mammalian  
MCH1 receptor is a rat MCH1 receptor.

25 102. A pharmaceutical composition which comprises an  
amount of a mammalian MCH1 receptor agonist  
determined by the process of claim 98 effective to  
increase activity of a mammalian MCH1 receptor and  
a pharmaceutically acceptable carrier.

30 103. A pharmaceutical composition of claim 102, wherein  
the mammalian MCH1 receptor agonist is not  
previously known.

35 104. A pharmaceutical composition which comprises an  
amount of a mammalian MCH1 receptor antagonist  
determined by the process of claim 99 effective to  
reduce activity of a mammalian MCH1 receptor and  
a pharmaceutically acceptable carrier.

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105. A pharmaceutical composition of claim 104, wherein the mammalian MCH1 receptor antagonist is not previously known.

5 106. A process for determining whether a chemical compound specifically binds to and activates a mammalian MCH1 receptor, which comprises contacting cells producing a second messenger response and expressing on their cell surface the  
10 mammalian MCH1 receptor, wherein such cells do not normally express the mammalian MCH1 receptor, with the chemical compound under conditions suitable for activation of the mammalian MCH1 receptor, and measuring the second messenger response in the  
15 presence and in the absence of the chemical compound, a change in the second messenger response in the presence of the chemical compound indicating that the compound activates the mammalian MCH1 receptor.

20 107. The process of claim 106, wherein the second messenger response comprises chloride channel activation and the change in second messenger is an increase in the level of inward chloride  
25 current.

30 108. A process for determining whether a chemical compound specifically binds to and inhibits activation of a mammalian MCH1 receptor, which comprises separately contacting cells producing a second messenger response and expressing on their cell surface the mammalian MCH1 receptor, wherein such cells do not normally express the mammalian MCH1 receptor, with both the chemical compound and  
35 a second chemical compound known to activate the

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mammalian MCH1 receptor, and with only the second chemical compound, under conditions suitable for activation of the mammalian MCH1 receptor, and measuring the second messenger response in the presence of only the second chemical compound and in the presence of both the second chemical compound and the chemical compound; a smaller change in the second messenger response in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound indicating that the chemical compound inhibits activation of the mammalian MCH1 receptor.

109. The process of claim 108, wherein the second messenger response comprises chloride channel activation and the change in second messenger response is a smaller increase in the level of inward chloride current in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound.

110. A process of any of claims 106, 107, 108, or 109, wherein the mammalian MCH1 receptor is a human MCH1 receptor or a mutant of such human MCH1 receptor which is activated by MCH or an analog or homolog thereof.

111. A process of any of claims 106, 107, 108, or 109, wherein the mammalian MCH1 receptor is a rat MCH1 receptor.

112. The process of any of claims 106, 107, 108, 109, or 110, wherein the cell is an insect cell.

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125. A method of screening a plurality of chemical compounds not known to inhibit the activation of a mammalian MCH1 receptor to identify a compound which inhibits the activation of the mammalian MCH1 receptor, which comprises:

(a) contacting cells transfected with and expressing the mammalian MCH1 receptor with the plurality of compounds in the presence of a known mammalian MCH1 receptor agonist, under conditions permitting activation of the mammalian MCH1 receptor;

(b) determining whether the activation of the mammalian MCH1 receptor is reduced in the presence of the plurality of compounds, relative to the activation of the mammalian MCH1 receptor in the absence of the plurality of compounds; and if so

(c) separately determining the inhibition of activation of the mammalian MCH1 receptor for each compound included in the plurality of compounds, so as to thereby identify the compound which inhibits the activation of the mammalian MCH1 receptor.

126. A method of claim 125, wherein the mammalian MCH1 receptor is a human MCH1 receptor or a mutant of such human MCH1 receptor which is activated by MCH or an analog or homolog thereof.

127. A method of claim 125, wherein the mammalian MCH1 receptor is a rat MCH1 receptor.

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128. A method of any of claims 123, 124, 125, 126, or 127, wherein the cell is a mammalian cell.
129. A method of claim 128, wherein the mammalian cell is non-neuronal in origin.
130. The method of claim 129, wherein the non-neuronal cell is a COS-7 cell, a 293 human embryonic kidney cell, a LM(tk-) cell or an NIH-3T3 cell.
131. A pharmaceutical composition comprising a compound identified by the method of claim 123 or 124 effective to increase mammalian MCH1 receptor activity and a pharmaceutically acceptable carrier.
132. A pharmaceutical composition comprising a compound identified by the method of claim 125 or 126 effective to decrease mammalian MCH1 receptor activity and a pharmaceutically acceptable carrier.
133. A method of treating an abnormality in a subject wherein the abnormality is alleviated by increasing the activity of a mammalian MCH1 receptor which comprises administering to the subject an amount of a compound which is a mammalian MCH1 receptor agonist effective to treat the abnormality.
134. A method of claim 133, wherein the abnormality is a regulation of a steroid or pituitary hormone disorder, an epinephrine release disorder, a gastrointestinal disorder, a cardiovascular disorder, an electrolyte balance disorder,

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135. A method of treating an abnormality in a subject wherein the abnormality is alleviated by decreasing the activity of a mammalian MCH1 receptor which comprises administering to the subject an amount of a compound which is a mammalian MCH1 receptor antagonist effective to treat the abnormality.
136. A method of claim 135, wherein the abnormality is a regulation of a steroid or pituitary hormone disorder, an epinephrine release disorder, a gastrointestinal disorder, a cardiovascular disorder, an electrolyte balance disorder, hypertension, diabetes, a respiratory disorder, asthma, a reproductive function disorder, an immune disorder, an endocrine disorder, a musculoskeletal disorder, a neuroendocrine disorder, a cognitive disorder, a memory disorder, a sensory modulation and transmission disorder, a

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MCH1 receptor or a mutant of such human MCH1 receptor which is activated by MCH or an analog or homolog thereof.

5      146.      The process of any of claims 142, 143, or 144, wherein the mammalian MCH1 receptor is a rat MCH1 receptor.

10      147.      A process for determining whether a chemical compound is a human MCH1 receptor antagonist which comprises contacting cells transfected with and expressing DNA encoding the human MCH1 receptor with the compound in the presence of a known human MCH1 receptor agonist, under conditions permitting the activation of the human MCH1 receptor, and detecting a decrease in human MCH1 receptor activity, so as to thereby determine whether the compound is a human MCH1 receptor antagonist, wherein the DNA encoding the human MCH1 receptor comprises the sequence shown in Figure 1 (Seq. ID No. 1) or contained in plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197), the known human MCH1 receptor agonist is MCH or a homolog or analog of MCH, and the cells do not express the MCH1 receptor prior to transfecting them.

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30      148.      A process for determining whether a chemical compound specifically binds to and inhibits activation of a human MCH1 receptor, which comprises separately contacting cells expressing on their cell surface the human MCH1 receptor and producing a second messenger response upon activation of the human MCH1 receptor, wherein such cells do not normally express the human MCH1 receptor and the DNA encoding the human MCH1

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receptor comprises the sequence shown in Figure 1 (Seq. ID No. 1) or contained in plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197), with both the chemical compound and a second chemical compound known to activate the human MCH1 receptor, and with only the second chemical compound, under conditions suitable for activation of the human MCH1 receptor, and measuring the second messenger response in the presence of only the second chemical compound and in the presence of both the second chemical compound and the chemical compound, a smaller change in the second messenger response in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound indicating that the chemical compound inhibits activation of the human MCH1 receptor, wherein the second chemical compound is MCH or a homolog or analog of MCH.

149. The process of claim 148, wherein the second messenger response comprises chloride channel activation and the change in second messenger response is a smaller increase in the level of inward chloride current in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound.

150. A method of screening a plurality of chemical compounds not known to inhibit the activation of a human MCH1 receptor to identify a compound which inhibits the activation of the human MCH1 receptor, which comprises:

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154. The process of any of claims 147, 148 or 150,  
5 wherein the cell is a COS-7 cell, a CHO cell, a  
293 human embryonic kidney cell, a NIH-3T3 cell,  
a mouse Y1 cell, or a LM(tk-) cell.

155. A process for making a composition of matter which specifically binds to a human MCH1 receptor which comprises identifying a chemical compound which specifically binds to the human MCH1 receptor and then synthesizing the chemical compound or a structural and functional analog or homolog thereof, wherein the chemical compound is identified as binding to the human MCH1 receptor by a process involving competitive binding which comprises contacting cells expressing on their cell surface the human MCH1 receptor, with both the chemical compound and a second chemical compound known to bind to the receptor, and separately with only the second chemical compound, under conditions suitable for binding of both compounds, and detecting the extent of specific binding of the chemical compound to the human MCH1 receptor, a decrease in the binding of the second chemical compound to the human MCH1 receptor in the presence of the chemical compound indicating that the chemical compound binds to the human MCH1 receptor, wherein the cells do not normally express the human MCH1 receptor, the human MCH1 receptor is encoded by nucleic acid comprising the sequence shown in Figure 1 (Seq. ID No. 1) or contained in plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197), and the second chemical compound is

156. A process for making a composition of matter which specifically binds to a human MCH1 receptor which comprises identifying a chemical compound which specifically binds to the human MCH1 receptor and then synthesizing the chemical compound or a structural and functional analog or homolog thereof, wherein the chemical compound is identified as binding to the human MCH1 receptor by a process involving competitive binding which comprises contacting a membrane preparation from cells expressing on their cell surface the human MCH1 receptor, with both the chemical compound and a second chemical compound known to bind to the receptor, and separately with only the second chemical compound, under conditions suitable for binding of both compounds, and detecting the extent of specific binding of the chemical compound to the human MCH1 receptor, a decrease in the binding of the second chemical compound to the human MCH1 receptor in the presence of the chemical compound indicating that the chemical compound binds to the human MCH1 receptor, wherein the cells do not normally express the human MCH1 receptor, the human MCH1 receptor is encoded by nucleic acid comprising the sequence shown in Figure 1 (Seq. ID No. 1) or contained in plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197), and the second chemical compound is MCH or a homolog or analog of MCH.

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5 a human MCH1 receptor antagonist and then  
synthesizing the chemical compound or a structural  
and functional analog or homolog thereof, wherein  
the chemical compound is identified as a human  
MCH1 receptor antagonist by a process which  
comprises contacting cells transfected with and  
expressing DNA encoding the human MCH1 receptor  
with the compound in the presence of a known human  
MCH1 receptor agonist, under conditions permitting  
10 the activation of the human MCH1 receptor, and  
detecting a decrease in human MCH1 receptor  
activity, so as to thereby determine whether the  
compound is a human MCH1 receptor antagonist,  
wherein the cells do not normally express the  
human MCH1 receptor, the human MCH1 receptor is  
15 encoded by nucleic acid comprising the sequence  
shown in Figure 1 (Seq. ID No. 1) or contained in  
plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197),  
and the known human MCH1 receptor agonist is MCH  
or a homolog or analog of MCH.

158. A process for making a composition of matter which  
specifically binds to and inhibits the activation  
of a human MCH1 receptor which comprises  
25 identifying a chemical compound which specifically  
binds to and inhibits the activation of the human  
MCH1 receptor and then synthesizing the chemical  
compound or a structural and functional analog or  
homolog thereof, wherein the chemical compound is  
30 identified as binding to and inhibiting the  
activation of the human MCH1 receptor by a process  
which comprises separately contacting cells  
expressing on their cell surface the human MCH1  
receptor and producing a second messenger response  
35 upon activation of the human MCH1 receptor,

wherein such cells do not normally express the human MCH1 receptor and the human MCH1 receptor is encoded by nucleic acid comprising the sequence shown in Figure 1 (Seq. ID No. 1) or contained in plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197), with both the chemical compound and a second chemical compound known to activate the human MCH1 receptor, and with only the second chemical compound, under conditions suitable for activation of the human MCH1 receptor, and measuring the second messenger response in the presence of only the second chemical compound and in the presence of both the second chemical compound and the chemical compound, a smaller change in the second messenger response in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound indicating that the chemical compound inhibits activation of the human MCH1 receptor, wherein the second chemical compound is MCH or a homolog or analog of MCH.

159. The process of claim 158, wherein the second messenger response comprises chloride channel activation and the change in second messenger response is a smaller increase in the level of inward chloride current in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound.

160. A process for preparing a composition which comprises identifying a chemical compound which specifically binds to a human MCH1 receptor, and then admixing a carrier and the chemical compound

or a structural and functional analog or homolog thereof, wherein the chemical compound is identified as binding to the human MCH1 receptor by a process involving competitive binding which comprises contacting cells expressing on their cell surface the human MCH1 receptor, with both the chemical compound and a second chemical compound known to bind to the receptor, and separately with only the second chemical compound, under conditions suitable for binding of both compounds, and detecting the extent of specific binding of the chemical compound to the human MCH1 receptor, a decrease in the binding of the second chemical compound to the human MCH1 receptor in the presence of the chemical compound indicating that the chemical compound binds to the human MCH1 receptor, wherein the cells do not normally express the human MCH1 receptor, the human MCH1 receptor is encoded by nucleic acid comprising the sequence shown in Figure 1 (Seq. ID No. 1) or contained in plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197), and the second chemical compound is MCH or a homolog or analog of MCH.

161. A process for preparing a composition which comprises identifying a chemical compound which specifically binds to a human MCH1 receptor, and then admixing a carrier and the chemical compound or a structural and functional analog or homolog thereof, wherein the chemical compound is identified as binding to the human MCH1 receptor by a process involving competitive binding which comprises contacting a membrane preparation from cells expressing on their cell surface the human MCH1 receptor, with both the chemical compound and

a second chemical compound known to bind to the receptor, and separately with only the second chemical compound, under conditions suitable for binding of both compounds, and detecting the extent of specific binding of the chemical compound to the human MCH1 receptor, a decrease in the binding of the second chemical compound to the human MCH1 receptor in the presence of the chemical compound indicating that the chemical compound binds to the human MCH1 receptor, wherein the cells do not normally express the human MCH1 receptor, the human MCH1 receptor is encoded by nucleic acid comprising the sequence shown in Figure 1 (Seq. ID No. 1) or contained in plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197), and the second chemical compound is MCH or a homolog or analog of MCH.

162. A process for preparing a composition which comprises identifying a chemical compound which is a human MCH1 receptor antagonist, and then admixing a carrier and the chemical compound or a structural and functional analog or homolog thereof, wherein the chemical compound is identified as a human MCH1 receptor antagonist by a process which comprises contacting cells transfected with and expressing DNA encoding the human MCH1 receptor with the compound in the presence of a known human MCH1 receptor agonist, under conditions permitting the activation of the human MCH1 receptor, and detecting a decrease in human MCH1 receptor activity, so as to thereby determine whether the compound is a human MCH1 receptor antagonist, wherein the cells do not normally express the human MCH1 receptor, the

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second chemical compound than in the presence of only the second chemical compound indicating that the chemical compound inhibits activation of the human MCH1 receptor, wherein the second chemical compound is MCH or a homolog or analog of MCH.

164. The process of claim 163, wherein the second messenger response comprises chloride channel activation and the change in second messenger response is a smaller increase in the level of inward chloride current in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound.

165. The process of any of claims 155, 156, 157, 158, 160, 161, 162, or 163, wherein the cell is an insect cell.

166. The process of any of claims 155, 156, 157, 158, 160, 161, 162, or 163, wherein the cell is a mammalian cell.

167. The process of claim 166, wherein the mammalian cell is nonneuronal in origin.

168. The process of claim 167, wherein the nonneuronal cell is a COS-7 cell, a 293 human embryonic kidney cell, a CHO cell, a NIH-3T3 cell, a mouse Y1 cell, or a LM(tk-) cell.

169. A method of treating an eating disorder or obesity in a subject which comprises administering to the subject a therapeutically effective amount of an MCH1 antagonist which inhibits the activation of

the MCH1 receptor.

170. A method of claim 169, wherein the MCH1 antagonist additionally inhibits the activation of the MCH1 receptor with an antagonist potency which is at least 30-fold greater than the antagonist potency with which the MCH1 antagonist inhibits the activation of each of the 5-HT2C and MC-4 receptors.

171. A method of claim 170, wherein the MCH1 antagonist additionally inhibits the activation of the MCH1 receptor with an antagonist potency which is at least 10-fold greater than the antagonist potency with which the MCH1 antagonist inhibits the activation of each of the NPY1, NPY5, GALR1, GALR2, and GALR3 receptors.

172. A method of claim 170, wherein the MCH1 antagonist additionally inhibits the activation of the MCH1 receptor with an antagonist potency which is at least 100-fold greater than the antagonist potency with which the MCH1 antagonist inhibits the activation of each of the 5-HT2C and MC-4 receptors.

173. A method of claim 172, wherein the MCH1 antagonist additionally inhibits the activation of the MCH1 receptor with an antagonist potency which is at least 100-fold greater than the antagonist potency with which the MCH1 antagonist inhibits the activation of each of the NPY1, NPY5, GALR1, GALR2, and GALR3 receptors.

174. A method of claim 169, wherein the MCH1 antagonist

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additionally binds to the MCH1 receptor with a binding affinity which is at least 10-fold greater than the binding affinity with which the MCH1 antagonist binds to each of the NPY1, NPY5, GALR1, GALR2, and GALR3 receptors.

180. A method of claim 178, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 100-fold greater than the binding affinity with which the MCH1 antagonist binds to each of the 5-HT2C and MC-4 receptors.

181. A method of claim 180, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 100-fold greater than the binding affinity with which the MCH1 antagonist binds to each of the NPY1, NPY5, GALR1, GALR2, and GALR3 receptors.

182. A method of claim 169, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 30-fold greater than the binding affinity with which the MCH1 antagonist binds to the dopamine D2 receptor.

183. A method of claim 169, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 30-fold greater than the binding affinity with which the MCH1 antagonist binds to the histamine H1 receptor.

184. A method of claim 169, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 100-fold

greater than the binding affinity with which the MCH1 antagonist binds to the dopamine D2 receptor.

185. A method of claim 169, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 100-fold greater than the binding affinity with which the MCH1 antagonist binds to the histamine H1 receptor.

186. A method of claim 169, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 200-fold greater than the binding affinity with which the MCH1 antagonist binds to the dopamine D2 receptor.

187. A method of claim 169, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 200-fold greater than the binding affinity with which the MCH1 antagonist binds to the histamine H1 receptor.

188. A method of claim 169, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 10-fold greater than the binding affinity with which the MCH1 antagonist binds to the  $\alpha_{1A}$  adrenoceptor.

189. A method of claim 169, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 100-fold greater than the binding affinity with which the MCH1 antagonist binds to the  $\alpha_A$  adrenoceptor.

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190. A method of claim 169, wherein the MCH1 antagonist additionally binds to the  $\alpha_{1A}$  adrenoceptor with a binding affinity which is no more than 10-fold greater than the binding affinity with which the MCH1 antagonist binds to the MCH1 receptor.

191. A method of claim 169, wherein the MCH1 antagonist additionally binds to the  $\alpha_{1A}$  adrenoceptor with a binding affinity which is no more than 100-fold greater than the binding affinity with which the MCH1 antagonist binds to the MCH1 receptor.

192. A method of treating an eating disorder in a subject which comprises administering to the subject a therapeutically effective amount of an MCH1 agonist which activates the MCH1 receptor.

193. A method of claim 192, wherein the MCH1 agonist additionally activates the MCH1 receptor with an agonist potency which is at least 30-fold greater than the agonist potency with which the MCH1 agonist activates each of the 5-HT<sub>2C</sub> and MC-4 receptors.

194. A method of claim 193, wherein the MCH1 agonist additionally activates the MCH1 receptor with an agonist potency which is at least 10-fold greater than the agonist potency with which the MCH1 agonist activates each of the NPY1, NPY5, GALR1, GALR2, and GALR3 receptors.

195. A method of claim 193, wherein the MCH1 agonist additionally activates the MCH1 receptor with an agonist potency which is at least 100-fold greater than the agonist potency with which the MCH1

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agonist activates each of the 5-HT<sub>2C</sub> and MC-4 receptors.

196. A method of claim 195, wherein the MCH1 agonist additionally activates the MCH1 receptor with an agonist potency which is at least 100-fold greater than the agonist potency with which the MCH1 agonist activates each of the NPY1, NPY5, GALR1, GALR2, and GALR3 receptors.

197. A method of any one of claims 192, 193, 194, 195, or 196, wherein the eating disorder is anorexia nervosa.

198. A method of treating depression and/or anxiety in a subject which comprises administering to the subject a composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a MCH1 antagonist, wherein:

- (a) (1) the MCH1 antagonist does not inhibit the activity of central monoamine oxidase A greater than 50 percent, at a concentration of 10mM; and (2) the MCH1 antagonist does not inhibit the activity of central monoamine oxidase B greater than 50 percent, at a concentration of 10mM; and
- (b) the MCH1 antagonist binds to the MCH1 receptor with a binding affinity at least ten-fold higher than the binding affinity with which it binds to each of the following transporters: serotonin transporter, norepinephrine transporter, and dopamine transporter.

199. The method of claim 198, wherein the MCH1 antagonist also binds to the MCH1 receptor with a binding

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affinity at least ten-fold higher than the binding affinity with which it binds to each of the human 5HT<sub>1A</sub>, human 5HT<sub>1B</sub>, human 5HT<sub>1D</sub>, human 5HT<sub>1E</sub>, human 5HT<sub>1F</sub>, human 5HT<sub>2A</sub>, rat 5HT<sub>2C</sub>, human 5HT<sub>4</sub>, human 5HT<sub>6</sub> and human 5HT<sub>7</sub> receptors.

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200. The method of claim 198, wherein the MCH1 antagonist also binds to the MCH1 receptor with a binding affinity at least ten-fold higher than the binding affinity with which it binds to the human histamine H<sub>1</sub> and H<sub>2</sub> receptors.

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201. The method of claim 198, wherein the MCH1 antagonist also binds to the MCH1 receptor with a binding affinity at least ten-fold higher than the binding affinity with which it binds to the human dopamine D<sub>1</sub>, D<sub>2</sub>, D<sub>3</sub>, D<sub>4</sub> and D<sub>5</sub> receptors.

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202. The method of claim 198, wherein the MCH1 antagonist also binds to the MCH1 receptor with a binding affinity at least ten-fold higher than the binding affinity with which it binds to the human  $\alpha_{1A}$  adrenoceptor, the human  $\alpha_{1B}$  adrenoceptor and the human  $\alpha_{1D}$  adrenoceptor.

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203. The method of claim 198, wherein the MCH1 antagonist also binds to the MCH1 receptor with a binding affinity at least ten-fold higher than the binding affinity with which it binds to the human  $\alpha_{2A}$  adrenoceptor, the human  $\alpha_{2B}$  adrenoceptor and the human  $\alpha_{2C}$  adrenoceptor.

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204. The method of claim 198, wherein the MCH1 antagonist does not inhibit the activity of central monoamine oxidase A greater than 60 percent.

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205. The method of claim 198, wherein the MCH1 antagonist does not inhibit the activity of central monoamine oxidase B greater than 60 percent.

206. The method of claim 198, wherein the MCH1 antagonist does not inhibit the activity of central monoamine oxidase A greater than 70 percent.

10 207. The method of claim 198, wherein the MCH1 antagonist does not inhibit the activity of central monoamine oxidase B greater than 70 percent.

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